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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,256	12/12/2003	Stephen M. Strittmatter	2159.0420002/EJH/SAC	9794

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,256	STRITTMATTER ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 23, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 31-66* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

Applicant's amendment filed December 23, 2005 is acknowledged. Claims 1-4 and 6-30 are cancelled. Claim 5, and newly added claims 31-66 are pending in this application. Claim 5 is withdrawn and new claims 31-66 are under examination in light of NgR2. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action (mailed September 29, 2005).

The correction of claim 22 in the rejection under 35 USC §101 in the previous office action is acknowledged.

Claim Rejections/Objections Withdrawn

The rejection of Claims 1-4, 8-10, and 22 under 35 U.S.C. 101 as lacking either a specific and substantial asserted utility or a well established utility is withdrawn in response to Applicant's amendment. Applicant argues that NgR2 has specific, substantial and credible utility (see pages 10-17, filed December 23, 2005) and has provided affidavits (submitted on December 23, 2005) to support the arguments. Applicant showed that NgR2 is able to bind to MAG in regulating neurite outgrowth. The extracellular domain of NgR2 can promote neurite outgrowth by binding to MAG to block the activity of MAG in inhibition of axonal outgrowth. In addition, Applicant argues that the polynucleiotides/polypeptides of NgR2 can be used for diagnosis and potential

treatment for CNS diseases. Applicant's arguments with respect to the rejection of claims 1-4, 8-10, and 22 have been fully considered and are persuasive. Thus, the rejection of claims 1-4, 8-10, and 22 under 35 U.S.C. 101, as lacking a specific and substantial asserted utility or a well established utility has been withdrawn.

The rejection of claims 1-4, 8-10, 22 with respect to new claims 31-66 under U.S.C 112 first paragraph as lacking total enablement is withdrawn in response to Applicant's amendment. Applicant argues that NgR2 has specific, substantial and credible utility by providing evidence of Exhibits 1 and 2, see pages 16-17, filed December 23, 2005. Applicant showed that the Fc-fusion protein with the extracellular domain of NgR2 is able to bind to MAG-Fc fusion protein and can reverse the inhibition of neurite outgrowth mediated by MAG-Fc fusion protein. Applicant's arguments with respect to the rejection of claims 1-4, 8-10, 22 and new claims 31-66 have been fully considered and are persuasive. Thus, the rejection of claims 1-4, 8-10, and 22 with respect to new claims 31-66 under 35 U.S.C.§ 112, first paragraph, as lacking total enablement has been withdrawn.

Claim Rejections/Objections Maintained/New Grounds of Rejection

The rejection of claims 1-4, 8-10, and 22 under 35 U.S.C. §112, first paragraph, because the specification would not be enabling for molecules of limited homology to the disclosed sequence is applied to new claims 31-33, 35-46 and 48-66 for reasons of record in the office action of September 29, 2005.

Applicant argues that claims are directed to variants or fragments of SEQ ID NO:2 that have a particular activity, which is to modulate inhibition of axonal elongation (p. 19). Applicant argues that the specification provides considerable guidance about what types of amino acids could be changed without affecting the function of the claimed polypeptides in modulating inhibition of axonal elongation by mutagenesis (p. 19-21). Applicant also argues that the motif of multiple leucinerich repeats in the NgR family is well known in the art, and refers to the article of Kobe et al. (TIBS, 1994, 19: 415-421) that the reference provides detailed information of the leucine-rich repeats in different proteins and the structural integrity of these proteins in contribution of their function. Applicant argues that the teachings in the specification do provide enough guidance for skilled artisans to envision the structures and functions of the claimed inventions, which include all of the polynucleotide sequence variants. Further, Applicant argues that the instant specification teaches how to make the variants and how to test the functions of variants.

Applicant argues that the claims do require a particular activity. However, Applicant hasn't taught what is required for that particular activity; i.e. we don't know what we could change and what we could not for that particular activity. Applicant argues that the specification provides guidance as to what could be changed. It is not found persuasive because the specification just teaches a lot of conservative substitutions. Applicant provides no direction as to how many could be made/changed or where they could be made without affecting activity. Further, Applicant argues that there is a lot known about the leucine-rich repeats and cites Kobe et al. to indicate that

the reference teaches us about what can be changed. It is not found persuasive. Although Kobe et al. teach that the common structure of the consensus residues of leucine-rich repeats and several proteins that contain these leucine-rich repeats, Kobe et al. also disclose that the function of these proteins is mostly due to the specific compositions of non-consensus residues within the proteins and is also influenced by the length of the repeats and the flanking domains (see p. 419, first column, fourth paragraph, in the section of LRR-containing proteins: functional and evolutionary similarities). Therefore, Kobe et al. do not teach what can be changed and what can not be changed in a polypeptides comprising at least 80% identity of the amino acids 1-310 of SEQ ID NO:2 to preserve the functional activity. Furthermore, Applicant argues that the specification teaches how to make mutations. However, the specification still has not taught us which ones to make. Finally, Applicant argues that the specification teach how to screen the variants. However, Applicant needs to provide the guidance as to how we are able to predict which ones would work. The guidance should be in light of how to "make and use", not how to "make and screen". Applicant's arguments have been fully considered but they are not persuasive. Thus, the rejection of claims 1-4, 8-10, and 22 under 35 U.S.C. §112, first paragraph, as the specification would not be enabling for molecules of limited homology to the disclosed sequence, which is applied to new claims 31-33, 35-46 and 48-66 is maintained.

The rejection of claims 1-3, 8-10, and 22 under 35 U.S.C.§ 112, first paragraph, as failing to meet the written description is applied to the newly added claims 31-33, 35-46, and 48-66 for reasons of record in the office action of September 29, 2005.

Applicant argues that the skilled artisan can envision the structural and functional features in the fragments containing the claimed polypeptides or variants because the sequence conservation in the NgR family as recited in the specification at p. 46, which is the leucine-rich repeats is known in the art and refers to the article of Kobe et al. This is not found persuasive. The claims are drawn to polynucleotides and a method of making polypeptides, which encompass variants and sequences comprising fragments that could vary widely in structure and function. Since there is no guidance as to what could be changed and what could not be changed to preserve any common characteristics in a polypeptide containing the sequence other than amino acids 1-310 of SEQ ID NO:2 and the sequences with at least 80% identity, the structural/functional features of these polypeptides are unpredictable. In addition, Applicant is not in possession of all polynucleotides comprising a polynucleotide encoding for at least 80% identity of the polypeptide of amino acids 1-310 of SEQ ID NO:2, which includes unknown sequences. Applicant may be in possession of NgR1-3 and may be enabled to modify the sequences consisting of NgR1-3 or fusion proteins of NgR1-3 consisting of the amino acids 1-310 of SEQ ID NO:2 and the sequence of Fc, GST, His or AP. However, Applicant is not in possession of a polypeptide comprising sequences other than NgR1-3. Furthermore, Applicant refers to the reference of Kobe et al. to support the argument that Applicant is in possession of the claimed inventions. It is not found

persuasive because Kobe et al. only discloses the conserved consensus residues of the leucine-rich repeats and proteins that contain these leucine-rich repeats. The reference of Kobe et al. does not support the argument that Applicant is in possession of all polynucleotides comprising a polynucleotide encoding for at least 80% identity of the polypeptide of amino acids 1-310 of SEQ ID NO:2. Applicant is not actually in possession of all polynucleotides comprising a polynucleotide encoding for at least 80% identity of the polypeptide of amino acids 1-310 of SEQ ID NO:2, One of ordinary skill in the art can not envision what other sequences are encompassed in the claimed polynucleotides and whether the claimed variant polynucleotides still maintain the capability to modulate inhibition of axonal elongation. Therefore, the rejection of claims 1-3, 8-10, and 22 under 35 U.S.C.§ 112, first paragraph, as failing to meet the written description, which is applied to the newly added claims 31-33, 35-46, and 48-66 is still maintained.

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
February 28, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

Considered CYW 2/1/06

Binding of myelin ligand to rNgR1 and huNgR2, 3 fusion protein

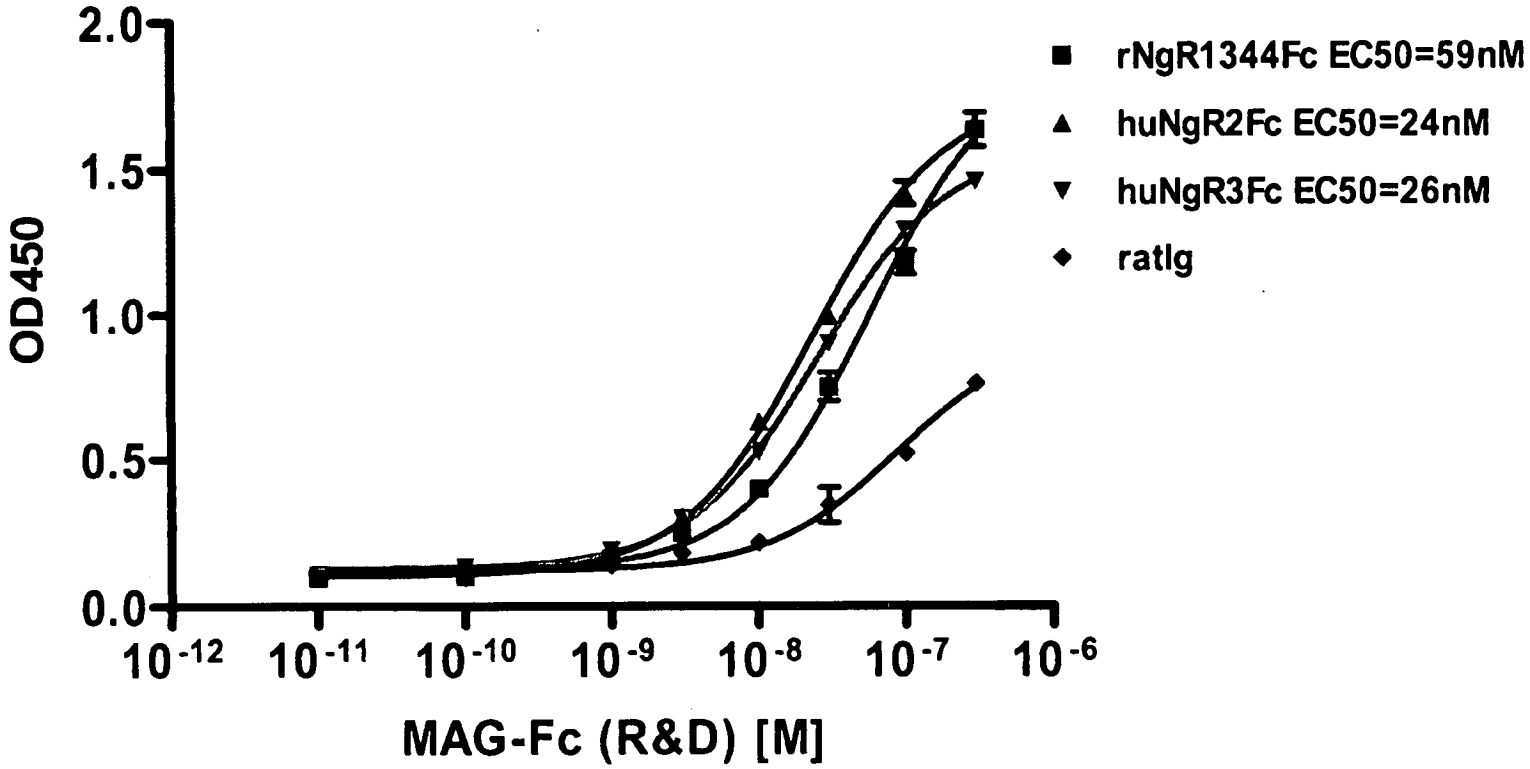
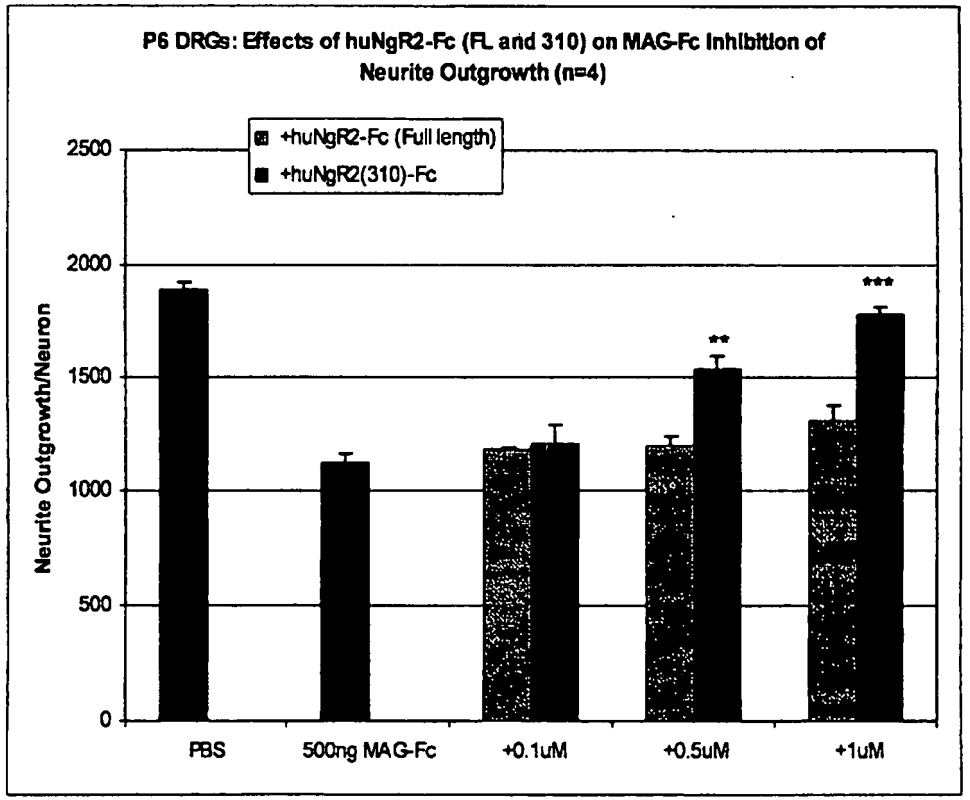


Exhibit 1
10/735,256

Considered CYW 2/7/06

huNgR2-(310)Fc promotes neurite outgrowth in a dose-dependent manner and to near control at 1uM on MAG-Fc



*p<0.05

**p<0.005

***p<0.0005

One-way Anova

Jirik 7-21-2005

Exhibit 2
10/735,256